

REMARKS

The present claims are 32-47. The present claims represent subject matter of canceled claims 19-31, rewritten in order to more clearly define the instant invention. New claims 45-47 define the "support" of claims 32, 36, and 41 attached to a "nucleotide monomer."

The previous claims of record have been redrafted and submitted as new claims 32-44 to address a number the alleged occurrences of indefinite claim language appearing in the statement of rejection under 35 U.S.C. 5112, second paragraph, in the Office action. Applicants respectfully submit that the newly submitted claims, along with the remarks, below, overcome the rejection.

The term "including" is no longer found in the claims. The term "comprising" is used, appropriately, as a transitional phrase in the instant claims. Comments contained in the Office Action to the contrary notwithstanding, the manner in which the term is used in a claim determines how the term is to be construed. When used as the "transitional phrase" of a claim, "comprising" renders the claim open to the inclusion of non-recited elements. *In re Janakirma-Rao*, 135 USPQ 893 (CCPA 1963); *Ex parte Davis*, 80 USPQ 448 (POBdApp 1948). Accordingly, the term is not limited to "refer to chemical compounds of known or knowable structure," as alleged in the statement of rejection. Moreover, applicants are free to be their own lexicographers. *In re Castaing*, 186 USPQ 550 (CCPA 1970). *In re Zletz*, 13 USPQ2d 1320 (Fed. Cir. 1989).

With respect to the functional language considered objectionable in claim 18, applicants have used more structural language in instant claim 32; that is, "a divalent hydrocarbon radical containing first and second adjacent carbon atoms, said first adjacent carbon atom bonded to a hydroxy group and said second adjacent carbon atom bonded to a nucleophilic group that can cleave a 3' or 5' phosphate, phosphite or phosphorothioate group from a nucleotide monomer through a one step β -elimination reaction."

With respect to the term "moiety," the examiner considers it indefinite because it is a generic term; that is, it is allegedly indefinite because "specific structural characteristics of the 'moiety'" are not recited. The fact that "moiety" is a broad term does not render it indefinite under § 112, since "breadth is not to be equated with indefiniteness." *In re Miller*, 169 USPQ 597, 600 (CCPA 1970). While it might be a broad term, "moiety" has a definite accepted meaning in the chemical arts.

Concerning the "nucleophilic group" limitations (present claims 34 and 35), applicants respectfully submit there is no conflict. Claims 34 and 35 merely define alternative embodiments of the "nucleophilic group." The statement of rejection fails to explain the "conflicting perspectives" allegedly created by reciting these alternative embodiments and, moreover, fails to explain how such alleged conflicting perspectives fail to satisfy the requirements of § 112 of the statute.

As for the allegedly *vague* language in claim 24, the language is not identified, other than by referring to it as being "very broad functional language similar in

vagueness to that of claim 18." Other than the fact that claim 24 depends (indirectly) on claim 18, there is no *functional* language in claim 24. Should the examiner wish to maintain the rejection of claim 24 on this basis, applicants respectfully request that the Examiner specifically identify the language considered indefinite.

Concerning reference to a "C-acetyl group or an O-acetyl group," the statement or rejection fails to explain how there is any relevance with respect to § 112, second paragraph, of the statute, since these terms are not found *in the claims*. 35 U.S.C. § 112, second paragraph, is applicable to only words found in the claims. *See, Ex parte Erlich*, 3 USPQ2d 1011 (BPAI 1987).

As to the caution against using process limitations in claims defining a composition of matter, the examiner's attention is respectfully directed to the decision of *In re Bridgeford*, 140 USPQ 55, 58 (CCPA 1966), which held that process limitations are *proper* in a claim that defines a composition of matter.

With respect to the language for "inert" groups, new claim 36 has been drafted to conform to the examiner's suggestion.

With respect to "heterocycle formed in part . . ." being indefinite, again, the allegation relates to the breadth of the claim, which cannot be made the basis of a § 112, 2nd paragraph rejection. *Miller*. Also, the claims now read "said divalent hydrocarbon radical forms part of a heterocycle." With respect to the limitation in claim 29, allegedly having the "same problem," applicants respectfully submit that the limitation is definite, structurally. One of ordinary skill in the art, certainly,

understands what is intended by a "cyclic moiety"; and, taken in conjunction with the formula recited in the claim (claim 29), the skilled artisan would understand how the "cyclic moiety" can be formed in "part" by the two substituents R_1 and R_2 .

As to the "conflicting perspectives on the nature of the 'nucleophile'" allegedly appearing in the claims, neither what is intended by "perspectives on the nature of a nucleophile" nor how these so-called perspectives are in conflict is explained in the statement of rejection. Applicants submit that the claims in question merely define different embodiments for the generic "heterocycle."

With respect to the term "Ac," the statement of rejection maintains that the term could mean either *acyl* or *acetyl*. With all due respect, the statement of rejection is incorrect; both claims 24 and 25 (as well as the present claims) expressly recite that "Ac" is an "acyl" group. (Emphasis added).

As to the use of functional language, overall, in the claims being considered objectionable, the claims cannot be rejected as indefinite on this basis. *In re Roberts*, 176 USPQ 313, 315 (CCPA 1973).

Claims are rejected under 35 U.S.C. 102 based on Vu or Lyttle. The examiner agreed, on the record (paper number 8, serial number 08/591,466, Interview Summary, page 2), that these references are not available as prior art against the instant claims. Withdrawal of these rejections is requested.

Claims are rejected under 35 USC 102 based on Webb or Nelson. Reconsideration is respectfully requested.

Applicants submit that neither Webb nor Nelson anticipate or even suggest a solid support presenting the structural features of the invention presently claimed. The present invention is drawn to a solid support for nucleic acid synthesis which comprises a hydrocarbon radical with two distinct reactive groups bound to two adjacent carbon atoms. These two reactive groups are:

- a hydroxy group (for the attachment and elongation of the nucleotide chain),
- and
- a nucleophilic group capable of cleaving a 3' or 5' phosphate, phosphite or phosphorothioate group from a nucleotide monomer through a one step β -elimination reaction.

As a consequence, once solid phase synthesis of an oligonucleotide is completed, only one reaction step is needed to both cleave the oligonucleotide from the solid support and generate a nucleotide sequence bearing a 3' or 5' terminal hydroxy group (see page 13, lines 14-20, and page 14 of the original application as filed). A structure providing for a single step cleavage and generation of a terminal hydroxy group is important, as prior art supports require a first reaction step to remove the oligonucleotide from the support and a second reaction step to obtain a hydroxy substituent at the terminal nucleotide.

Webb describes a support for oligonucleotide synthesis, which comprises a nucleoside -linker coupled to a polymer. Webb does not teach a solid support harboring a nucleophilic group capable of the one step β -elimination cleavage of the

support from the nucleotide. To the contrary, Webb uses a nucleophilic group to obtain a covalent bond between the nucleoside-linker and a polymer prior to the attachment and elongation of the nucleotide on the support (see column 3, lines 44-54). Webb et al. is completely silent on the particular chemical properties and resulting structural requirements of the nucleophilic groups used in the present invention. Webb does not disclose or suggest a solid support comprising a hydroxy group and a nucleophilic group on adjacent carbons wherein said nucleophilic group is capable of β -elimination. It is precisely this structural requirement, which confers one the present invention's greatest attributes, the ability to cleave the oligonucleotide from the solid support, such that the terminal phosphate group remains on the support any thereby generating an oligonucleotide with a free hydroxy group at the terminal nucleotide. Moreover, the particular structure to which the Examiner draws attention at the bottom of column two is not a completed "support for the synthesis of a nucleic acid," but rather an intermediate in the synthesis of the Webb support.

Nelson et al. generally concerns a support useful in solid phase oligonucleotide synthesis. In particular, Nelson describes a support allowing the synthesis of a 3' amino-modified oligonucleotide (see pages 7187-7188). This reference does not describe or suggest a support comprising a nucleophilic group capable of β -elimination. The oligonucleotides obtained with the support described in Nelson et al. invariably bear an additional functional group at their 3' terminus instead of the terminal OH

group that would have been generated by a nucleophilic group capable of β -elimination as described in the present invention.

With respect to the figure 1 of the Nelson reference, to which the examiner refers at page 8 of the Office action, applicants submit that this structure does not meet the requirements for a solid supports of the present invention. Nelson does not describe or suggest a nucleophilic group that can cleave a 3' or 5' phosphate, phosphite or phosphorothioate group from a nucleotide monomer through a one step β -elimination. It is also to be noted that, neither Webb nor Nelson teach or suggest, a solid support comprising the cyclic moiety required in claims 41-44 (corresponding to previous claims 23-31).

Furthermore, applicants respectfully submit that the rejection based on Webb is improper on its face. The statement of rejection refers to passages from Webb "all of which strongly *suggest anticipation* of Applicant's invention" (emphasis added). A prior art reference cannot *suggest* anticipation; anticipation requires that each and every limitation of the claim be found in a single prior art reference arranged in the same manner as in the claim. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). The statement of rejection fails to show how each and every claim limitation is present in the reference, as arranged in the claim. An argument by the PTO is "not prior art." *In re Rijckaert*, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). When the "PTO asserts that there is an explicit or implicit teaching or

suggestion in the prior art, it must indicate where such a teaching or suggestion appears *in the reference*." 28 USPQ2d at 1557, *emphasis added*.

With respect to the rejection of previous claims 23-31 (corresponding to present claims 41-44), the invention presently claimed is independently patentable over either Webb or Nelson. The structural formulae recited in these claims do not read on any material either expressly or inherently described in these references. Irrespective of any functional limitations, the structural limitations recited in claims 41-44 (and found in previous claims 23-31), alone, demonstrate that neither reference anticipates these claims. With all due respect, the statement of rejection fails to address *all* of the rejected claims. The only reasoning provided to support the rejections is the alleged appearance of vague and broad functional language in the claims; however, there were, and are, claims containing structural definitions, and the statements of rejection do not explain how these limitations could be fully met in either of the cited references. Accordingly, these claims are independently patentable over the art cited.

Claims were, further, rejected under 35 USC 103 based on Arnold(I) (US5362866). Reconsideration is respectfully requested.

Arnold does not teach a solid support comprising a hydroxy group (for the attachment and elongation of the nucleotide chain) and a nucleophilic group capable of cleaving a 3' or 5' phosphate, phosphite or phosphorothioate group from a nucleotide through a one step β -elimination reaction.

Figure 1 of the Arnold reference shows that, once the synthesis is completed, the oligonucleotide released from the solid support by oxidation carries a phosphate group at its terminus instead of a hydroxy substituent. Arnold is completely silent on the inclusion of a nucleophilic group that can cleave a 3' or 5' phosphate. This is further illustrated by Example 4 of the Arnold reference describing oxidative removal of oligonucleotides from the solid support, which is chemically quite distinct from a β -elimination.

It is further submitted that Arnold (see bottom of column 1 and top of column 2) suggests the motivation for the present invention but does not suggest the solid supports described in the present application. Indeed, the present invention concerns a support for the solid phase synthesis of nucleic acids, which can be used irrespective of the first DNA or RNA nucleotide to be synthesized, and which still permits a convenient release of the nucleic acid once the synthesis is completed. However, Arnold describes a radically different support used in a radically different process, and therefor fails to anticipate or render obvious the present invention. In fact, Arnold's appreciation of the motivation for the present invention, but failure to grasp any part of it, is evidence of the present invention's lack of obviousness.

Additionally, the rejection is based on the *claims* of the Arnold patent. A patent's claims are no measure of what a patent discloses for prior art purposes of 35 USC 103. *In re Benno*, 226 USPQ 683 (Fed. Cir. 1985).

Moreover, the statement of rejection is based on alleged similarities between the claimed *process* of Arnold and the process of making the presently claimed "support." That is, the statement of rejection seems to rely on the misperception that the process claimed by Arnold *inherently* produces the "support" presently claimed. With all due respect, the statement of rejection fails to satisfy the requirements for a showing of obviousness under § 103.

Inherency is a doctrine well established in patent law. For a disclosed structure to *inherently* contain a particular property "it must be "inevitable" from the prior art disclosure. *In re Wilding*, 190 USPQ 59, 62 (CCPA 1976). "In relying on a theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990), emphasis in original.

The statement of rejection fails to provide the requisite "technical reasoning" to establish that the Arnold process *inevitably* must effect the presently claimed "support." All that is stated is that Arnold "claims a process for making compounds of the *kind apparently envisioned* by the instant claims and therein [inherently] discloses compounds which appear to be encompassed by the instant claims" (emphasis added). Assuming, *arguendo*, that the Arnold process is the "*kind*" of process used to make the presently claimed "support," it is not the *identical* process. Lacking *identity* of processes, *inevitability of identical products* is not established; any

difference in the processes could, theoretically, result in different products being produced.

Finally, there is no showing that the Arnold process is, in fact, the "kind apparently envisioned by the instant claims," let alone the identical process. The statement of rejection relies on a bare allegation, without any supporting scientific reasoning, or comparison with the Arnold disclosure, other than a mere reference to Arnold's "claims." An argument by the PTO is "not prior art." *Rijckaert*, 28 USPQ2d at 1557. When the

PTO asserts that there is an explicit or implicit teaching or suggestion in the prior art, it must indicate where such a teaching or suggestion appears *in the reference*. ... The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient to establish inherency. ... [S]uch a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection.

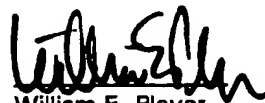
28 USPQ2d at 1557, *emphasis added*.

Moreover, as with the rejections based on Webb or Nelson, the invention defined in previous claims 23-31, and present claims 41-44, is independently patentable over Arnold. The structural formulae recited in these claims do not read on any material either expressly or inherently described Arnold; and, the statement of rejection is based on the alleged appearance of vague and broad functional language in the claims.

Favorable action commensurate with the foregoing is requested.

Respectfully submitted,

By:



William E. Player
Reg. No. 31,409

JACOBSON, PRICE, HOLMAN & STERN, PLLC
400 Seventh Street, N.W.
The Jenifer Building
Washington, D.C. 20004
Tel.: (202) 638-6666
Atty. Dkt. No.: P60188US1

S:\HOME\CBROWN\FER\P60188U1.AMD